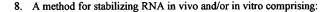
- (B) TITLE: Analysis of the nucleotide sequence of chromosome VI from Saccharomyces cerevisiae.
- (C) JOURNAL: Nature Genet.
- (D) VOLUME: 10
- (H) PAGES: 261-268
- (I) DATE:1995
- (J) RELEVANT RESIDUES IN SEQ ID NO. 1: 1097-1118

(vii) SEQUENCE DESCRIPTION: SEQ ID NO.2:

TTGTGGTGAA CGATAGATGG AC

What is claimed is:

- 1. A method for generating phosphorothioate oligo mixtures comprising:
 - 1) growing a single-stranded recombinant DNA phage in modified media that uses thiophosphate as a source of phosphate
 - 2) harvesting the single-stranded phage and purifying the DNA corresponding to the recombinant DNA insert
 - 3) fragmentation of the insert DNA such that oligo mixtures spanning the entire length of the segment are generated.
- The method of claim 1 used to generate phosphorothioate ds DNA, ss DNA, and/or RNA by in vivo incorporation of thio-phosphate into nucleotide precursor pools.
- The method of claim 1 used to generate ds DNA, ss DNA, or RNA partially substituted with
 phosphorothioate linkages by culturing cells in media consisting of a mixture of thio-phosphate and
 inorganic phosphate.
- The method of claim 1 wherein the cells cultured in thio-phosphate media are of prokaryotic or eukaryotic origin.
- 5. The method of claim 1 using other derivatives of phosphate such as those substituted with one or more sulfur group, methyl group or other moiety.
- A method for increasing the natural mutation rate of organisms, particularly, prokaryotes by culturing or growth in media utilizing thio-phosphate as a source of phosphorous.
- 7. The method of claim 6 used to selectively mutate phage or plasmid DNA comprising:
 - 1)several rounds of phage or plasmid amplification with host cells cultured in the presence of thio-phosphate containing media
 - 2) harvesting the phage or plasmid DNA after each cycle of amplification
 - 3)infecting or transforming new host cells each cycle of amplification.



- 1) the growth of prokaryotic or eukaryotic cells in media containing thio-phosphate as a source of phosphorous
- the subsequent isolation of the RNA by rapid boiling, or organic extraction methods and/or RNA binding matrices.
- 9. The method of claim 8 where the introduction of thio-phosphate into multicellular organisms is accomplished by ... tion, digestion, or absorption.
- 10. The method of claim 8 used to maximize the accumulation of a desired protein product(s) comprising:
 - 1) growing cells in thio-phosphate containing media
 - 2) determining the optimal ratio of thio-phosphate to inorganic phosphate in the culture media
 - 3) determining the optimal time point for maximum levels of protein synthesis.
- 11. The method of claim 10 wherein the cells used to generate the protein are prokaryotic or eukaryotic in origin.
- 12. The method of claim 10 wherein the protein is produced using a recombinant DNA expression vector.
- 13. The method of claim 10 wherein the enhancement of a protein or several proteins is used to increase the rate or yield of non-protein products such as antibiotics, chemical intermediates, organic acids, etc.

 $\langle \ \rangle$